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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Gunnar Plesch

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EXAMINER

COLLINS, CYNTHIA E

ART UNIT

PAPER NUMBER

1638

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DELIVERY MODE

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/566,644	PLESCH ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 28 April 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-21, 25 and 27-30 is/are pending in the application.
- 4a) Of the above claim(s) 1, 6-21, 25 and 27-30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2-5 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 31 January 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☒ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>3306.41706</u>  | 6) <input type="checkbox"/> Other: _____                          |

**DETAILED ACTION*****Election/Restrictions***

Applicant's election with traverse of Group 194, claims 2(a)-(e) and (i), and claims 3-5, corresponding to SEQ ID NO: 1 or nucleic acid encoding SEQ ID NO: 2 in the reply filed on April 28, 2008 is acknowledged.

The traversal is on the ground(s) that 35 U.S.C. 121 requires that inventions be independent *and* distinct to be restrictable.

This is not found persuasive because an application may properly be required to be restricted to one of two or more claimed inventions if they are either independent *or* distinct (MPEP § 803). It is also noted that because the instant application is a national stage application filed under 35 USC 371, the restriction requirement must be (and was) predicated on unity of invention or lack thereof.

The traversal is also on the ground(s) that there is no undue burden on the Examiner to search at least all the groups corresponding to the elected sequence together.

This is not found persuasive because while the search of the groups corresponding to the elected sequence may overlap, their searches are not coextensive of each other. In this particular instance, a search of the nonelected groups corresponding to the elected sequence is not coextensive with a search of Group 194 since Group 1 requires a search for increasing or generating the biological activity of a protein, and Group 388 requires a search for monoclonal antibodies against a polypeptide, which searches are not required for the invention of group 194.

The requirement is still deemed proper and is therefore made FINAL.

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Claims 1, 6-21, 25 and 27-30, and the nonelected sequences and subject matter, are withdrawn from consideration.

### *Specification*

The abstract of the disclosure is objected to because it lacks proper content.

Applicant is reminded of the proper content of an abstract of the disclosure.

A patent abstract is a concise statement of the technical disclosure of the patent and should include that which is new in the art to which the invention pertains. If the patent is of a basic nature, the entire technical disclosure may be new in the art, and the abstract should be directed to the entire disclosure. If the patent is in the nature of an improvement in an old apparatus, process, product, or composition, the abstract should include the technical disclosure of the improvement. In certain patents, particularly those for compounds and compositions, wherein the process for making and/or the use thereof are not obvious, the abstract should set forth a process for making and/or use thereof. If the new technical disclosure involves modifications or alternatives, the abstract should mention by way of example the preferred modification or alternative.

The abstract should not refer to purported merits or speculative applications of the invention and should not compare the invention with the prior art.

Where applicable, the abstract should include the following:

- (1) if a machine or apparatus, its organization and operation;
- (2) if an article, its method of making;
- (3) if a chemical compound, its identity and use;
- (4) if a mixture, its ingredients;
- (5) if a process, the steps.

Extensive mechanical and design details of apparatus should not be given.

Correction of the abstract is required. See MPEP § 608.01(b).

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

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The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The abstract of the disclosure is objected to because it lacks a reference to and brief description of the drawing(s) as set forth in 37 CFR 1.74.. Correction is required.

See MPEP § 608.01(b).

The disclosure (Figure 1) is objected to because of the following informalities: the disclosure does not comply with 37 CFR 1.182, which requires that reference be made to a sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application. Appropriate correction is required.

### ***Claim Objections***

Claims 2-5 are objected to because of the following informalities: the claims are directed in part to nonelected inventions. Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was

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not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims require the use or manipulation of at least one nucleic acid molecule comprising a nucleic acid molecule consisting of: a) a nucleic acid molecule encoding of the polypeptide as depicted in SEQ ID NO:2, b) a nucleic acid molecule comprising of the nucleic acid molecule as depicted in SEQ ID NO: 1, c) a nucleic acid molecule whose sequence can be deduced from a polypeptide sequence encoded by a nucleic acid molecule of (a) or (b) as a result of the degeneracy of the genetic code and conferring an increase in the amount of fine chemical in an organism or a part thereof; d) a nucleic acid molecule which encodes a polypeptide which has at least 50% identity with the amino acid sequence of the polypeptide encoded by the nucleic acid molecule of (a) to (c) and conferring an increase in the amount of fine chemical in an organism or a part thereof; e) a nucleic acid molecule which hybridizes with a nucleic acid molecule of (a) to (c) under stringent hybridization conditions and conferring an increase in the amount of fine chemical in an organism or a part thereof; i) nucleic acid molecule which is obtainable by screening a suitable nucleic acid library under stringent hybridization conditions with a probe comprising, one of the sequences of the nucleic acid molecule of (a) to (k) or with a fragment thereof having at least 15 nt, preferably 20 nt, 30 nt, 50 nt, 100 nt, 200 nt or 500 nt of the nucleic acid molecule characterized in (a) to (k) and conferring an increase in the amount of the fine chemical in an organism or a part thereof, or comprising a sequence which is complementary thereto.

The instant claims thus encompass methods that use or manipulate a genus of polynucleotides that are functionally defined as conferring an increase in the amount of the fine chemical in an organism or a part thereof, and that are structurally defined as encoding SEQ ID NO:2, as comprising SEQ ID NO:1, as encoding a polypeptide having at least 50% identity with the amino acid sequence of SEQ ID NO:2, as hybridizing to such sequences under undefined stringency conditions, as being obtainable by screening a suitable nucleic acid library under undefined stringency conditions with a probe comprising such sequences or their fragments having at least 15 to 500 nucleotides, and as being complementary to such sequences.

A sequence listing is provided for SEQ ID NOs: 1 (DNA) and 2 (protein). The specification describes SEQ ID NO:1 as a 579 bp DNA sequence obtained from *Saccharomyces cerevisiae* that encodes a polypeptide having the amino acid sequence of SEQ ID NO:2 (sequence listing; page 11). The specification also notes that SEQ ID NO:1 as has been published and is named as rho2, a gene that encodes a non-essential GTPase of the rho/rac subfamily of the ras-like GTPase that may play a role in the establishment of cell polarity or in microtubule assembly (page 11). The specification additionally suggests that the gene product of SEQ ID NO:1 (the RHO2 protein) could be used for the production of a fine chemical, meaning of preferably for the production of essential amino acids, in particular for increasing the amount of an essential amino acid in free or bound form in an organism or a part thereof, meaning that the increase of its biological activity by overexpression of the responsible gene could lead to an increase of a fine chemical (page 11).

The specification also indicates that “fine chemicals” encompasses “Certain products and by-products of naturally-occurring metabolic processes in cells have utility in a wide array of industries, including, but not limited to, the food, feed, cosmetics, and pharmaceutical industries and agriculture” (page 1). Since the specification at page 1 broadly defines “fine chemicals” without specific structural or functional limitations, the claims are sufficiently broad to encompass the production of any type of chemical molecule in an organism.

The specification does not describe the actual production of any type of chemical molecule in any type of organism in which the expression of the nucleic acid sequence of SEQ ID NO:1 is increased or generated. The specification also does not describe nucleotide sequences that function to confer an increase in the amount of a fine chemical in an organism or a part thereof and that encode a polypeptide having at least 50% identity with the amino acid sequence of SEQ ID NO:2, or that hybridize to nucleotide sequences that encode a polypeptide having at least 50% identity with the amino acid sequence of SEQ ID NO:2, or that were obtained by screening a nucleic acid library.

The Federal Circuit has clarified the application of the written description requirement to nucleic acid sequences. The court stated that “A description of a genus of cDNAs may be achieved by means of recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus.” See *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1569; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court has also affirmed the PTO's applicable standard for determining compliance with the written description



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requirement, quoting from the PTO's Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, P1, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106, where it is set forth that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ... i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." See *Enzo Biochem Inc. v. Gen-Probe Inc.*, 63 USPQ2d 1609, 1613 (CAFC 2002)

In the instant case Applicant has not described a representative number of species falling within the scope of the genus of sequences required to practice the claimed invention which encompasses polynucleotides that function to confer an increase in the amount of the fine chemical in an organism or a part thereof and that encode a polypeptide having at least 50% identity with the amino acid sequence of SEQ ID NO:2, or that hybridize to nucleotide sequences that encode a polypeptide having at least 50% identity with the amino acid sequence of SEQ ID NO:2, or that were obtained by screening a nucleic acid library. Applicant also has not described detailed, relevant identifying characteristics sufficient to conclude that the applicant was in possession of the genus of sequences required to practice the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2, and claims 3-5 dependent thereon, are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission

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amounting to a gap between the steps. See MPEP § 2172.01. Claim 2 is directed to a process for the production of fine chemical comprising increasing or generating in an organism or a part thereof the expression of at least one nucleic acid molecule comprising a nucleic acid molecule, but claim 2 recites no positive method steps by which this may be accomplished.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2, 3 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Qadota H. et al. (RHO gene products, putative small GTP-binding proteins, are important for activation of the CAL1/CDC43 gene product, a protein geranylgeranyltransferase in *Saccharomyces cerevisiae*. Yeast. 1992 Sep;8(9):735-41).

Claim 2(a)-(e) and (i) is drawn to a process for the production of fine chemical comprising increasing or generating in an organism or a part thereof the expression of at least one nucleic acid molecule comprising a nucleic acid molecule consisting of: a) a nucleic acid molecule encoding of the polypeptide as depicted in SEQ ID NO:2, b) a nucleic acid molecule comprising of the nucleic acid molecule as depicted in SEQ ID NO: 1, c) a nucleic acid molecule whose sequence can be deduced from a polypeptide sequence encoded by a nucleic acid molecule of (a) or (b) as a result of the degeneracy of the genetic code and conferring an increase in the amount of fine chemical in an

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organism or a part thereof; d) a nucleic acid molecule which encodes a polypeptide which has at least 50% identity with the amino acid sequence of the polypeptide encoded by the nucleic acid molecule of (a) to (c) and conferring an increase in the amount of fine chemical in an organism or a part thereof; e) a nucleic acid molecule which hybridizes with a nucleic acid molecule of (a) to (c) under stringent hybridization conditions and conferring an increase in the amount of fine chemical in an organism or a part thereof; i) nucleic acid molecule which is obtainable by screening a suitable nucleic acid library under stringent hybridization conditions with a probe comprising, one of the sequences of the nucleic acid molecule of (a) to (k) or with a fragment thereof having at least 15 nt, preferably 20 nt, 30 nt, 50 nt, 100 nt, 200 nt or 500 nt of the nucleic acid molecule characterized in (a) to (k) and conferring an increase in the amount of the fine chemical in an organism or a part thereof, or comprising a sequence which is complementary thereto.

Qadota H. et al. teach a process comprising increasing or generating by in the yeast *Saccharomyces cerevisiae* the expression of at least one nucleic acid molecule comprising a nucleic acid molecule consisting of a nucleic acid molecule (SEQ ID NO:1) encoding of the polypeptide (RHO2) as depicted in SEQ ID NO:2 (page 736 column 1; page 737 Figure 1; page 738 Table 1 and Figure 2). Qadota H. et al. also teach recovery of a free or bound fine chemical (the RAS2 protein, page 739 Figure 3).

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

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the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Qadota H. et al. (RHO gene products, putative small GTP-binding proteins, are important for activation of the CAL1/CDC43 gene product, a protein geranylgeranyltransferase in *Saccharomyces cerevisiae*. Yeast. 1992 Sep;8(9):735-41) in view of Monaghan E. et al. (Mutations in the Lcb2p subunit of serine palmitoyltransferase eliminate the requirement for the TSC3 gene in *Saccharomyces cerevisiae*. Yeast. 2002 Jun 15;19(8):659-70).

Claim 4 is drawn to the process of claim 2 further comprising the following steps: (a) selecting an organism or a part thereof expressing a polypeptide encoded by the nucleic acid molecule characterized in claim 2; (b) mutagenizing the selected organism or the part thereof; (c) comparing the activity or the expression level of said polypeptide in the mutagenized organism or the part thereof with the activity or the expression of said polypeptide of the selected organisms or the part thereof; (d) selecting the mutated organisms or parts thereof, which comprise an increased activity or expression level of said polypeptide compared to the selected organism or the part thereof; (e) optionally, growing and cultivating the organisms or the parts thereof; and (f) recovering, and optionally isolating, the free or bound fine chemical produced by the selected mutated organisms or parts thereof.

Qadota H. et al. teach the limitations of claim 2 as set forth above.

Qadota H. et al. do not teach the limitations of claim 4.

Monaghan E. et al. teach a process comprising selecting an organism (*Saccharomyces cerevisiae*) expressing a polypeptide (the Lcb2p subunit of SPT )

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encoded by a nucleic acid molecule; mutagenizing the selected organism; comparing the activity of said polypeptide in the mutagenized organism with the activity of said polypeptide of the selected organism; selecting the mutated organism which comprises an increased activity of said polypeptide compared to the selected organism (page 664-665 Figure 2; page 666 Figure 3; page 667 Figure 4).

It would have been *prima facie* obvious to one skilled in the art at the time the invention was made to make and select mutants of *Saccharomyces cerevisiae* that have an increased activity or expression level of the *Saccharomyces cerevisiae* RHO2 protein, given that the RHO2 protein and coding sequence were known at the time the invention was made (as evidenced by Qadota H. et al.), and given that methods for making and selecting mutants of *Saccharomyces cerevisiae* were well established in the art at the at the time the invention was made (as evidenced by Monaghan E. et al.). One skilled in the art would have been motivated to do so in order to functionally characterize the *Saccharomyces cerevisiae* RHO2 protein. One skilled in the art would have had a reasonable expectation of success, given the successful production of other gain of function mutants in *Saccharomyces cerevisiae*. Accordingly, one skilled in the art would have been motivated to generate the claimed invention with a reasonable expectation of success. Thus, the claimed invention would have been *prima facie* obvious as a whole to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

### ***Remarks***

No claim is allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Cynthia Collins/  
Primary Examiner, Art Unit 1638

CC